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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,897	12/29/2003	Anthony Joonkyoo Yun	PALO-002	7432

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EXAMINER

RAMACHANDRAN, UMAMAHESWARI

ART UNIT	PAPER NUMBER
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1617

MAIL DATE	DELIVERY MODE
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06/12/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/748,897	Applicant(s) YUN ET AL.	
	Examiner Umamaheswari Ramachandran	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 May 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 and 41 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-28 and 41 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION***Election/Restrictions***

Applicants' election of group XIII, claims 1-28, 41 in the reply filed on 3/23/2007 and election of species propranolol as beta blocker, NSAID as non beta blocker and aging associated condition and loss of parasympathetic function as sub species is acknowledged. Claims 29-40, 42-61 are withdrawn from consideration. The election has been made with traverse. The Applicants' argue that search and examination of the entire application can be made without serious burden. In response, the claims are directed to different conditions like, neuroinflammatory condition such as meningitis or orthopedic inflammatory condition such as Paget's disease, osteoporosis, gastrointestinal condition, transplant related condition and they are different and distinct disorders and have acquired a separate status in the art due to their recognized divergent subject matter and hence the inventions require a different field of search and the prior art applicable to one invention may not likely be applicable to another invention. The search for all inventions would place an undue burden on the Office in view of the corresponding diversity in the field of search for each group. Thus the restriction requirement elected is made final. Claims 1-28, 41 are pending.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

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F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 11, 12, 27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of 1-3, 30 of U.S. Patent No. (U.S. 7,149,574) ('574).

Claims 1, 11, 12, 27 instant application teaches a method of treating a subject for a condition caused by an autonomic nervous system abnormality comprising modulating at least a portion of said subject's autonomic nervous system by administering an effective amount of at least one beta blocker and with at least one electrode and applying electrical energy to treat conditions like inflammatory conditions, genitourinary conditions, infectious diseases gastrointestinal conditions, endocrine conditions, orthopedic inflammatory conditions, Th-2 dominant conditions, conditions that cause hypoxia, conditions that cause hypercarbia etc.

Claims 1, 11, 12 and 30 of the patent '574 teach a method of treating a subject for a condition caused by an abnormality in said subject's autonomic nervous system said method comprising electrically modulating at least a portion of said subject's autonomic nervous system and by the use of at least one pharmacological agent such

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as beta blocker to increase the parasympathetic activity/sympathetic activity ratio to treat conditions like inflammatory conditions, genitourinary conditions, infectious diseases gastrointestinal conditions, endocrine conditions, orthopedic inflammatory conditions, Th-2 dominant conditions, conditions that cause hypoxia, conditions that cause hypercarbia etc.

The patent does not teach a method of treating the elected species aging associated condition by a method of electrically modulating at least a portion of said subject's autonomic nervous system and by the use of at least one pharmacological agent such as beta blocker. However the group of conditions for aging associated condition includes shy dragger, age related inflammation conditions etc. (claim 41 of the instant application). However, the patent teaches a method of treating inflammatory conditions by a method comprising electrically modulating the subject's autonomic nervous system and the use of a pharmacological agent such as a beta-blocker. It is obvious to one of ordinary skill in the art that age related inflammation is an inflammatory condition and a method of treatment of the genus inflammatory condition would be therapeutically effective to treat any age related inflammation.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they are obvious variation of the patent.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 9, 10, 14, 16, 19-22, 28, 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Gambardella et al. (Metabolism, 46, 3, March, 1999, p 291-297).

Gambardella et al. teach a method of treating a condition due to deficient parasympathetic activity associated with elevated basal metabolic rate in cancer patients by oral administration of propranolol (see Abstract, p 295, para 1, lines 1-8, p 296, para 4, 1-5). The reference teaches the autonomic nervous system dysfunction in cancer patients with elevated basal metabolic rate, there is an unbalanced sympathetic (SNS)/parasympathetic nervous system (PNS) ratio which may exist due to SNS overactivity in cancer patients due to impaired PNS activity. The reference further teaches that beta-blocker such as propranolol administration may be useful to counteract the negative impact of the SNS on metabolic pathways (p 297, para 3 continued on 298). Hence the reference inherently teaches the sympathetic bias in at least a portion of autonomic nervous system, abnormality characterized by sympathetic bias, parasympathetic bias with an unbalanced SNS/PNS ratio with high SNS activity and low PNS activity

Claims 1-7, 9, 10, 21, 28, 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Brevetti et al. (Brief communications, Nov 1981, p 938-941).

Brevetti et al. teach an intravenous and oral administration of propranolol for the treatment of Shy-Drager syndrome, a severe degeneration of the autonomic nervous system. The reference further teaches that orthostatic hypotension a condition of Shy-Drager syndrome is mainly dependent on peripheral vasodilation without the normal

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response of postural vasoconstriction and may be a consequence of an imbalance of alpha and beta adrenoreceptor activity in peripheral nervous system and that beta-blockade may provide an effective means of treating orthostatic hypotension in patients with Shy-Drager syndrome (p 940 para 2, lines 1-5, continued on page 941). The reference teaches a sympathetic bias and a parasympathetic bias in at least a portion of said autonomic nervous system.

Claims 1, 21, 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Nordling et al. (E Urol, 1992, 21, 328-331).

Nordling et al. teach the administration of non-selective beta-adrenergic receptor antagonist propranolol reduced the urethral inflammation (see Abstract).

Claims 1-7, 9, 10-12, 15, 17, 21, 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Majcherczyk et al. (Br J Pharmacol, 1987, 91(4), 711-4).

Majcherczyk et al. teaches the increase in renal sympathetic nerve activity by propranolol in hypertensive rats (Abstract). Hypertension is an age-associated condition and the reference inherently teaches the sympathetic and non-sympathetic bias and a low sympathetic activity.

Claims 1, 21, 23-25, 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Davies et al. (The J of Intl Med Research, 1988, 16, 173-181).

Davies et al. teach the administration of ibuprofen, a non-steroidal anti-inflammatory drug along with an anti-hypertensive agent and a beta-blocker such as propranolol (see Abstract) to group of patients with hypertension. It is inherent that

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hypertension, an age-associated condition is common in elderly patients and parasympathetic nerves influence cerebral blood flow during hypertension.

Claims 1, 26-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Hill et al. (U.S. 6,449,507).

Hill et al. teach the stimulation of nerve or nerve fibers (vagus nerve fibers, hypoglossal nerve fibers, phrenic nerve fibers, parasympathetic nerve fibers, and sympathetic nerve fibers, a vagal nerve) by using electrodes and electrical current and further comprising beta-blockers such as propranolol in a medical procedure such as beating heart surgery, arrhythmias, vascular surgery, neurosurgery etc which are aging associated conditions (col. 2, lines 61-65, col. 17, claim 1, claim 10, col. 18, claim 19, co. 20, claim 50).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 8, 13, 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gambardella et al. (Metabolism, 46, 3, March, 1999, p 291-297).

Gambardella et al. teachings discussed as above. The reference does not teach a method of treating conditions caused by abnormality in autonomic nervous system wherein the abnormality is characterized by normal sympathetic activity or substantially

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equal parasympathetic and sympathetic functions in at least a portion of said autonomic nervous system.

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer a beta blocker such as propranolol in treating a condition caused by abnormality in autonomic nervous system where the abnormality is characterized by normal sympathetic activity or substantially equal parasympathetic and sympathetic functions in at least a portion of said autonomic nervous system. The motivation to do so is provided by Gambardella et al. The reference teaches that propranolol is effective in the treatment of abnormality in autonomic nervous system. Hence one of ordinary skill in the art would have been motivated to achieve the desired results and therapeutic effects upon administration of a beta-blocker as Gambardella et al has taught the safety of the drug and effectiveness of propranolol in treating the disorder associated with the abnormality of autonomic nervous system.

Conclusion

No Claims are allowed.

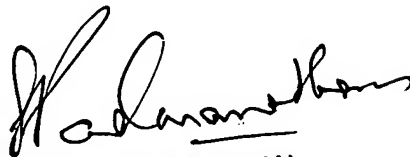
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone

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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER